

WHAT IS CLAIMED IS:

1 A method of treating or preventing immunodeficiency virus infection or a
consequence thereof in a human subject in need of such treatment or prevention comprising
5 administering to the subject an amount effective to treat or prevent immunodeficiency virus infection
or a consequence thereof of a composition comprising a variant, derivative, or analog of
lipopolysaccharide or lipid A, which variant or derivative or analog (a) exhibits substantially no
pyrogenicity or reduced pyrogenicity relative to lipopolysaccharide or lipid A, and (b) is active in
inducing the secretion of one or more β chemokines but exhibits decreased induction relative to
10 lipopolysaccharide and lipid A of one or more proinflammatory cytokines.

2. The method of claim 1 wherein the immunodeficiency virus is human
immunodeficiency virus.

15 3. The method of claim 2 which further comprises administering to the subject a
therapeutically effective amount of a chemokine.

4. The method of claim 3 which further comprises administering to the subject a
therapeutically effective amount of a chemokine selected from the group consisting of RANTES,
20 MIP-1 α and MIP-1 β .

5. The method of claim 2 which further comprises administering to the subject an anti-
viral drug other than a lipopolysaccharide or lipid A variant or analog or derivative of reduced or
absent pyrogenicity.
25

6. The method of claim 5 in which the anti-viral drug is selected from one or more of the
group consisting of AZT, 3TC, ddI, ddC, 3TC, and zidovudine.

7. The method of claim 5 in which the anti-viral drug is selected from a protease
30 inhibitor or a glycosylation inhibitor.

8. The method of claim 1 in which said lipopolysaccharide variant is administered, which variant is isolated from a gram negative bacterium.

5 9. The method of claim 8 in which the lipopolysaccharide variant is isolated from a gram negative microorganism containing at least one mutation in a gene selected from the group consisting of *kdsA*, *kdsB*, *htrB*, *msbB*, *lpx A*, *lpx B* and *kdt A*.

10 10. The method of claim 8 in which the lipopolysaccharide variant is obtained by a method comprising isolating a preparation containing lipopolysaccharide from a gram negative microorganism containing at least one mutation in one of the genes encoding myristoyl transferase or one of the genes encoding lauroyl transferase.

15 11. The method of claim 8 in which the lipopolysaccharide variant is obtained by a method comprising isolating a preparation containing lipopolysaccharide from a gram negative bacteria selected from the group consisting of: *Haemophilus influenzae*, *Escherichia coli*, *Salmonella enterica*, *Klebsiella pneumoniae*, *Bordella pertussis*, *Pseudomonas aeruginosa*, *Chlamydia psittaci*, and *Legionella pneumophila*.

20 12. The method of claim 8 in which the lipopolysaccharide variant is isolated from an *E. coli* strain *htrB1::Tn10 msbB::ωcam* double mutant.

25 13. The method of claim 8 in which the lipopolysaccharide variant is isolated from *Rhodobacter sphaeroides* or *Rhizobium leguminosarum*.

14. The method of claim 1 in which said derivative of a lipopolysaccharide is administered, which derivative is obtained by a method comprising modifying naturally occurring lipopolysaccharide.

30 15. The method of claim 2 in which said derivative of a lipopolysaccharide is

administered, which is a derivative obtained by a method comprising modifying naturally occurring lipopolysaccharide.

16. The method of claim 14 in which the derivative is obtained by treating a naturally
5 occurring lipopolysaccharide with acyloxyacyl hydrolase.

17. The method of claim 14 in which the derivative is obtained by subjecting a naturally occurring lipopolysaccharide to alkaline hydrolysis.

10 18. The method of claim 14 in which the derivative is obtained by subjecting a naturally occurring lipopolysaccharide to deacylation.

19. The method of claim 14 in which the derivative has a shortened carbon backbone relative to the lipopolysaccharide.

15

20. The method of claim 14 in which the derivative is modified in that one or more of the glucosamine residues are substituted with galactosamine residues.

21. The method of claim 14 in which the derivative is a nonphosphoryl or
20 monophosphoryl form of the lipopolysaccharide.

22. The method of claim 14 in which the derivative is in a purified form.

23. The method of claim 1 in which an analog is administered, which analog is a
25 synthetic analog of lipopolysaccharide or lipid A.

24. The method of claim 23 wherein the synthetic analog is lipid X.

25. The method of claim 23 wherein the synthetic analog is lipid IV_A.

30

26. The method of claim 23 wherein the synthetic analog contains a 2-deoxy-2-aminogluconate residue in place of the glucosamine-1-phosphate at the reducing end and bears a galacturonic acid moiety instead of a phosphate at position 4'.

5 27. The method of claim 23 wherein the synthetic analog contains the pentaacyl structure of the lipopolysaccharide found in *Rhodobacter sphaeroides*.

28. The method of claim 23 wherein the synthetic analog lacks phosphate and the glucosamine disaccharide is replaced by a different chemical structure.

10 29. The method of claim 2 wherein the composition comprises a first and second molecule selected from among said variant, derivative and analog, in which the first and second molecules differ.

15 30. The method of claim 1 wherein said composition further comprises a lipopolysaccharide or lipid A containing structure isolated from a gram-negative microorganism.

31. The method of claim 30 wherein said variant, derivative, or analog is a lipopolysaccharide antagonist, and said lipopolysaccharide antagonist is in molar excess of the
20 lipopolysaccharide or lipid A containing structure.

32. A method of screening a preparation comprising a variant, derivative or analog of lipopolysaccharide or lipid A, of reduced or absent pyrogenicity, for anti-immunodeficiency virus activity comprising assaying said preparation for the ability to inhibit immunodeficiency virus
25 replication or expression of immunodeficiency virus RNA or protein or to alleviate symptoms of an immunodeficiency virus-induced disorder.

33. The method of claim 32 in which the immunodeficiency virus is HIV.

30 34. The method of claim 33 in which the preparation is assayed by a method comprising

measuring HIV-1 p24 antigen levels in cultured hematopoietic cells acutely infected with HIV-1, which cells have been contacted with the preparation; and comparing the measured HIV-1 p24 antigen levels in the cells which have been contacted with the lipopolysaccharide preparation with said levels in cells not so contacted with the preparation, wherein a lower level in said contacted cells indicates that the preparation has anti-HIV activity.

35. The method of claim 33 in which the preparation is assayed by a method comprising measuring the activity of a reporter gene product expressed from a construct in which the HIV-1 LTR is operably linked to said reporter gene, wherein said construct is present in cultured cells which have been contacted with the preparation; and comparing the measured expression of said reporter gene in the cells which have been contacted with the preparation with said levels in such cells not so contacted, wherein a lower level in said contacted cells indicates that the preparation has anti-HIV activity.

36. The method of claim 33 in which the preparation is assayed by a method comprising measuring HIV-1 derived RNA transcripts or HIV-1 antigen levels in HIV-1 transgenic mice administered the preparation; and comparing the measured transcript or antigen levels in the mice which have been administered the preparation with said levels in mice not so administered, wherein a lower level in said administered mice indicates that the preparation has anti-HIV activity.

37. The method of claim 33 in which the preparation is assayed by a method comprising measuring SIV p27 antigen levels in the peripheral blood mononuclear cells of SIV infected monkeys administered the preparation; and comparing the measured antigen levels in the monkeys which have been administered the preparation with said levels in monkeys not so administered, wherein a lower level in said administered monkeys indicates that the preparation has anti-HIV activity.

38. A pharmaceutical composition comprising an amount effective to treat or prevent immunodeficiency virus infection of a preparation comprising a variant, derivative, or analog of lipopolysaccharide or lipid A, that exhibits reduced or absent pyrogenicity; and a pharmaceutically acceptable carrier.

39. The pharmaceutical composition of claim 38 which is formulated as a controlled release formula.

5 40. The pharmaceutical composition of claim 38 which further comprises a therapeutically effective amount of a chemokine.

41. The pharmaceutical composition of claim 40 in which the chemokine is one or more of the chemokines selected from the group consisting of RANTES, MIP-1 α and MIP-1 β .

10 42. The pharmaceutical composition of claim 38 in which the variant, derivative, or analog stimulates β chemokine secretion but does not stimulate pyrogenic cytokine release.

15 43. The pharmaceutical composition of claim 42 which is formulated as a controlled release formula.

44. The pharmaceutical composition of claim 42 which further comprises a therapeutically effective amount of a chemokine.

20 45. The pharmaceutical composition of Claim 37 which comprises a lipopolysaccharide variant isolated from a gram negative microorganism.

25 46. The pharmaceutical composition of claim 45 which is formulated as a controlled release formula.

47. The pharmaceutical composition of claim 45 which further comprises a therapeutically effective amount of a chemokine.

30 48. The pharmaceutical composition of claim 47 in which the chemokine is one or more of the chemokines selected from the group consisting of RANTES, MIP-1 α and MIP-1 β .

49. The pharmaceutical composition of Claim 45 in which the lipopolysaccharide variant is isolated from a gram negative microorganism containing at least one mutation in a gene selected from the group consisting of *kdsA*, *kdsB*, *htrB*, *msbB*, *lpx A*, *lpx B* and *kdt A*.

5

50. The pharmaceutical composition of claim 49 which is formulated as a controlled release formula.

51. The pharmaceutical composition of claim 49 which further comprises a therapeutically effective amount of a chemokine.

10

52. The pharmaceutical composition of claim 45 in which the lipopolysaccharide variant is isolated from an *E. coli* strain *htrB1::Tn10 msbB::ocam* double mutant.

15

53. The pharmaceutical composition of claim 52 which is formulated as a controlled release formula.

54. The pharmaceutical composition of claim 52 which further comprises a therapeutically effective amount of a chemokine.

20

55. The pharmaceutical composition of claim 37 which comprises said lipopolysaccharide derivative, in which the lipopolysaccharide derivative is derived from a modified naturally occurring lipopolysaccharide.

25

56. The pharmaceutical composition of claim 55 which is formulated as a controlled release formula.

57. The pharmaceutical composition of claim 55 which further comprises a therapeutically effective amount of a chemokine.

30

58. A pharmaceutical composition comprising an amount of lipid X or lipid IV_A effective to treat or prevent immunodeficiency virus infection; and a pharmaceutical carrier.

59. The pharmaceutical composition of claim 58 which is formulated as a controlled
5 release formula.

60. The pharmaceutical composition of claim 58 which further comprises a therapeutically effective amount of a chemokine.

10 61. The method of claim 2 in which the variant, derivative, or analog is in purified form.

62. The method of claim 9 in which the variant, derivative, or analog is in purified form.